administration, and also on the condition to be treated. For example, when the composition is formulated for oral administration, preferably in the form of a dosage unit such as a capsule, each dosage unit may preferably contain 1 μg to 5 mg of estrogenic and estrogenic modulatory molecules and 50 μg to 300 mg of progesterone. U.S. Patent No. 4,900,734 provides additional examples of acceptable dose combinations of estrogenic molecules and progestins.

Other uses involving electrically or magnetically active constituents

The compositions of the present invention have a number of additional uses aside from substance delivery. Embodiments exist in which the incorporation of electrically or magnetically active constituents in the electroprocessed material allows the electroprocessed material to move rhythmically in response to an oscillating electric or magnetic field. Such an electroprocessed material can be used, for example, in a left ventricular assist device by providing a pumping action or a ventricular massage to a heart patent. Oscillations can be accomplished by passive movement of a magnetic or electric field with respect to the conductive material, or vice versa. By manipulating material selection, the electroprocessed material can be designed to remain in place permanently or to dissolve over time, eliminating the need for surgery to recover the device once the heart had recovered sufficiently.

Embodiments also exist in which an implanted electroprocessed material is used to convey an electric charge or current to tissue. For example, electrically active constituents can be electrically stimulated to promote neural ingrowth, stem cell differentiation, or contraction of engineered muscle, or to promote the formation of bone in orthopedic applications in which electroprocessed material is used as a carrier to reconstruct bone. In one embodiment, for example, an electroprocessed material is applied to a bone injury site and used to apply an electric current to the material to facilitate and to promote healing. The application of a small electric current to an injured bone is known to accelerate healing or promote the healing of bone injuries.

In other embodiments involving magnetically reactive materials, a magnetic field is used to position an electroprocessed material containing substances by relatively non-invasive means, for example by directing the movement of the material within the peritoneum. In other embodiments, a composition containing electrically active compounds is used to produce electric

field-driven cell migration. This approach accelerates the healing process and minimize the risk of bacterial colonization. In one example, an orthopedic implant is coated with a very thin (< 100 microns) layer of an electrically active polymer. With a very thin electrode attached to the coating, upon post-implantation, an electric field can be applied via an external electrode such that the electric field-driven cell migration is towards the implant surface. The direction can be reversed if so desired. Field orientation depends on the geometry of the implant and external electrode.

Use in gene therapy

Compositions of the present invention are also useful for testing and applying various gene therapies. By working with the compositions *in vitro*, different types of gene therapy and manipulation can be achieved by inserting preselected DNA in suspensions of cells, materials, etc. For example, nonviral techniques such as electroporation are used to treat cultured cells prior to insertion into the matrix of the present invention. In other embodiments, cells are treated within the matrix before the composition is inserted into a recipient. *In vitro* gene transfer avoids the exposure of a recipient to viral products, reduces risk of inflammation from residual viral particles and avoids the potential for germ cell line viral incorporation. It avoids the problem of finding or engineering viral coats large enough to accept large genes such as the one for Factor VIII (anti-hemophilic factor). However, *in vivo* gene therapy is accomplished in some embodiments by, for example, incorporating DNA into the electroprocessed material as it is created through the electroprocessing techniques of the present invention, whereby some DNA will be incorporated into the *in vivo* cells in contact with the composition after application of the composition to the recipient. This is especially true of small gene sequences, such as antisense oligonucleotides.

Use of an electroprocessed composition as tissue or organ replacement

The ability to combine cells in an electroprocessed material provides the ability to use the compositions of the present invention to build tissue, organs, or organ-like tissue. Cells included in such tissues or organs can include cells that serve a function of delivering a substance, seeded cells that will provide the beginnings of replacement tissue, or both. Many types of cells can be used to

create tissue or organs. Stem cells, committed stem cells, and/or differentiated cells are used in various embodiments. Also, depending on the type of tissue or organ being made, specific types of committed stem cells are used. For instance, myoblast cells are used to build various muscle structures, neuroblasts are employed to build nerves, and osteoblasts are chosen to build bone. Examples of stem cells used in these embodiments include but are not limited to embryonic stem cells, bone marrow stem cells and umbilical cord stem cells used to make organs or organ-like tissue such as livers, kidneys, etc. Examples of tissue embodiments that use differentiated cells include fibroblasts in a matrix used for a patch, for example a hernia patch, endothelial cells for skin, osteoblasts for bone, and differentiated cells like cadaver donor pancreatic islet cells for a delivery device to place these cells in a specific site, for example the liver. In some embodiments the shape of the electroprocessed composition helps send signals to the cells to grow and reproduce in a specific type of desired way. Other substances (for example, differentiation inducers) can be added to the electroprocessed matrix to promote specific types of cell growth. Further, different mixtures of cell types are incorporated into the composition in some embodiments.

In certain disease states, organs are scarred to the point of being dysfunctional. A classic example is cirrhosis. In cirrhosis, normal hepatocytes are trapped in fibrous bands of scar tissue. In one embodiment of the invention, the liver is biopsied, viable liver cells are obtained then cultured in an electroprocessed matrix, and re-implanted in the patient as a bridge to or replacement for routine liver transplantations.

Mixing of committed cell lines in a three dimensional electroprocessed matrix can be used to produce structures that mimic complex organs. For example, by growing glucagon secreting cells, insulin secreting cells, somatostatin secreting cells, and/or pancreatic polypeptide secreting cells, or combinations thereof, in separate cultures, and then mixing them together with electroprocessed materials through electroprocessing, an artificial pancreatic islet is created. These structures are then placed under the skin, retroperitoneally, intrahepatically or in other desirable locations, as implantable, long-term treatments for diabetes.

In other examples, hormone-producing cells are used, for example, to replace anterior pituitary cells to affect synthesis and secretion of growth